DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

I-011468-A-0000

DEC 0 6 2006

U.S. Department of the Interior
Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Attention: David Erdahl, Ph.D.
Branch Chief, AADAP
4050 Bridger Canyon Road
Bozeman, MT 59715

Re: Request for an Investigational New Animal Drug exemption for channel catfish pituitary

Dear Dr. Erdahl:

We grant your request for the establishment of an Investigational New Animal Drug (INAD) exemption file for channel catfish pituitary (CP) injectable solution for catfish. Channel catfish pituitary is proposed for the induction of gamete maturation (ovulation and spermiation) in a variety of catfish species. Additionally, in your correspondence dated January 31, 2006, you requested authorization to slaughter for human food consumption 10,000 catfish treated with CP. You proposed an investigational withdrawal time of 10 days. Additionally, you requested a categorical exclusion from the requirement to prepare an environmental assessment in accordance with 21.CFR 25.33(e). You declared that, to your knowledge, no extraordinary circumstances exist which may significantly affect the human environment as discussed under 21 CFR 25.21.

For administrative purposes, we have assigned your file number INAD 011468 for the above referenced use of channel catfish pituitary in catfish. Please refer to this number in all drug shipments and correspondence concerning the drug while it is in investigational use.

AUTHORIZATION FOR THE USE OF EDIBLE PRODUCTS

We have completed our review and find that an investigational exemption for the use of channel catfish pituitary in catfish species is consistent with public health. Accordingly, we authorize you to (1) market for human food use the edible tissues derived from experimental animals or (2) release into public waters for possible human consumption experimental animals treated in the following manner:

AUTHORIZATION TABLE:

DRUG	Channel Catfish Pituitary
Dosage Form	Desiccated and powdered whole channel catfish pituitary
Route of Administration	Intraperitoneal (IP) or intramuscular (IM) injection in sterile saline
SPECIES	Catfish (various species)
Class	N/A
Number of Animals	10,000
MAXIMUM DOSE (or Range) **Frequency and Duration**	Up to 25 mg channel catfish pituitary/ kg bw total administered dose. The investigational drug may be administered up to two times in a 12 hr period, with the total administered dose not to exceed 25 mg/kg bw.
MINIMUM WITHDRAWAL PERIOD	A 3-day investigational withdrawal period is needed for fish receiving channel catfish pituitary. No investigational withdrawal period is required for offspring of fish receiving channel catfish pituitary.
COMMENTS	Concomitant therapy with approved new animal drugs, or investigational new animal drugs with an approved investigational food use authorization, will not affect the current food use authorization for channel catfish pituitary.
RENDERING	Fish receiving channel catfish pituitary may be rendered at any time.

The investigational withdrawal time may be reconsidered upon the receipt and review of additional information regarding the preparation of the channel catfish pituitary investigational product. The additional information should include details regarding the alcohol/acetone rinse solution, length of exposure of channel catfish pituitaries to the alcohol/acetone solution, the use of heat or vacuum in the drying process, and an estimate of the wet weight to dry weight ratio comparing fresh whole and desiccated powdered pituitaries. In addition, this information may be sufficient to satisfy any further human food safety (toxicology or residue) concerns for channel catfish pituitary.

ENVIRONMENTAL CONSIDERATIONS

We have reviewed the information in the INAD plus additional references pertaining to the use of hormones such as CP and the hybridization of channel with blue catfish. It is our understanding that only a limited amount of CP will be used in the experiments and the CP used is expected to be contained within the pond systems. Therefore, we agree with your claim that the investigational use of CP falls within the categorical exclusion under 21 CFR 25.33(e), and neither an environmental assessment (EA) or an environmental impact statement is required for the current investigation. This categorical exclusion from preparation of an EA and an Environmental Impact Statement does not relieve you of the responsibility for determining and meeting all Federal, State, and local environmental and occupational laws and regulations that apply to the manufacturing, use, and disposal of the investigational drugs. It will also be necessary to provide information on the possible impact of CP on the environment at the time a new animal drug application (NADA) is submitted for the product. Therefore, it is important to begin gathering information on the possible fate and effects of CP in the environment from the proposed use.

Additionally, based upon the information available to us, it appears that CP is necessary for the hybridization of channel with blue catfish. If this is the case, then information on the possible environmental impacts associated with the possible escape of the hybrid will also be necessary for the approval of an NADA for the proposed product. The issues presented in Smitherman, R. O. and R. A. Dunham in 1993 (Relationships Among Cultured and Naturally Occurring Populations of Freshwater Catfish in the United States. Proceedings of the 22nd U.S.-Japan Meeting on Aquaculture, Homer, Alaska, August 21-22, 1993. Marcia R. Collie and James P. McVey, Editors. Fairbanks, Alaska: University of Alaska Sea Grant College Program, [1995]. UJNR technical report; no. 22. Alaska sea grant report; AK-SG-95-03) concerning possible environmental impacts of the hybrid should be studied and included in an environmental assessment for the approval of an NADA for this product. Additionally, if information becomes available indicating that the hybrid represents a higher risk to the environment than initially believed, then the information should be considered relative to ongoing investigations. Methods for containing potentially fertile hybrids should be implemented and the appropriate federal, state, and local authorities for the release of exotic species (including hybrids) should be contacted.

INVESTIGATIONAL LABELING

You provided investigational labeling language to be included in the file. This labeling is consistent with the requirements set forth in 21 CFR 511.1(a) and (b). The investigational labeling should be affixed to your investigational drug product prior to shipment and this investigational label should be affixed, if possible, to each individual drug container.

The new animal drug regulations, Section 511.1(b)(3) and (4) require the sponsor to submit specific information prior to each shipment or other delivery of the drug for clinical investigation in animals. The drug shipment form which you submitted (Form CP-1) is acceptable for use.

Clinical investigations for this INAD cover only the treatment regimen stated above. Drugs given to control animals must be administered in full compliance with the currently approved

use. Your investigators should be made aware of their responsibilities under Section 511.1(b)(7)(ii) and Section 511.1(c)(1).

You should note that this authorization is for a specific number of fish in total. Additional numbers of animals may be requested in the future. Having a specific number of animals, rather than annual numbers, facilitates our tracking under the INAD. We remind you that an animal that has been treated more than once still only counts as a single animal toward the authorization. The investigational withdrawal time subsequent to the last treatment must be observed.

As you track the total number of animals used by your investigators, a request for additional animals should be made with sufficient lead time to allow us to process an amended authorization. Upon receipt of the letter containing an amended authorization, you may begin counting the number of animals used from zero.

In order for us to complete our files, the disposition of all investigational animals and unused drugs must be reported to this office, as well as adverse reactions observed. Please refer to this letter by date and INAD number when reporting the details of clinical investigations or the disposition of investigational animals.

ADDITIONAL COMMENTS

1. The protocol submitted has not received a formal review since it is not designed for a pivotal study; however, it appears to be adequate to begin your initial investigations. CVM encourages you to discuss study design issues and submit protocols to the Center for review prior to initiating a pivotal study.

2. The proposed claim of gamete maturation may be overly specific for the types of data to be collected. Gamete maturation and gamete release can be separate processes under the control of different hormones, depending on the fish species. Using the proposed claim of spawning aid, similar to the approved claim for human chorionic gonadotropin, with egg or milt release as the definition of a successful treatment, may allow for simpler study designs. Controlling for all the variables that may impact egg or milt maturation and release and those that affect the hatching and viability of fry may create very complicated study designs with multiple variables to be measured and evaluated to determine a treatment success.

3. Anesthesia is considered a concomitant therapy. If fish will be sedated or anesthetized for injection or stripping, this should be noted on data collection forms and in reports submitted to CVM.

4. We received your notification of a change in the study monitor via e-mail. The selection of Dr. Patricia Gaunt as study monitor is acceptable.

5. We remind you that an investigational new animal drug must be manufactured, processed, packaged, and labeled in such a way as to maintain appropriate standards of identity, strength, quality, and purity as needed for safety and to give significance to investigations made with the drug. According to CVM's current policy, as described in the Program Policy and Procedures Manual Guide 1240.4122, Sterility

and Pyrogen Requirements for Injectable Drug Products, all injectable drug products should be sterile except euthanasia products and ear implants for bovine and ovine species. Additionally, please note that additional studies may be required if the investigational formulation and the final formulation are not identical.

6. A product development plan should be submitted to demonstrate your and the drug manufacturer's intentions to develop the information necessary for a new animal drug application. The plan should contain a strategy and projected target dates for the completion of each technical section needed for approval. The technical sections include animal safety, effectiveness, human food safety, environmental safety, manufacturing chemistry and controls, all other information, and labeling. You should demonstrate due diligence toward meeting the technical section requirements as outlined in the development plan.

7. We recommend that you request a meeting with the Office of New Animal Drug Evaluation to further discuss your proposed claim and development plan for a new animal drug application (NADA). Requests for regulatory discretion, such as changes to the list of low regulatory priority aquaculture drugs in Guide 1240.4200, should be directed to Mrs. Fran Pell, HFV-235, Office of Surveillance and Compliance. For further information about indexing, please contact Dr. Meg Oeller, Office of Minor Use and Minor Species Animal Drug Development.

8. We remind you of the continued necessity to provide annual reports under the FDA/CVM Aquaculture Workload Plan. Your annual report should comprise: a) a brief summary of the past year's activities and accomplishments in each of the technical sections for the NADA; b) certification of accountability of all drugs shipped under the INAD, records maintenance for FDA inspection, compliance with the provisions of 21 CFR 511, including notification of adverse effects relative to humans, target animals, or the environment resulting from the use of the investigational drug; c) a list of all investigators, facilities, and species treated; and d) a copy of the current study protocol(s) noting any modification or revision.

If you submit correspondence relating to this letter, your correspondence should reference this letter and the principal submission identifier found at the top of this letter. If you have any questions about this letter, please contact Dr. Joan C. Gotthardt, Director, Division of Therapeutic Drugs for Food Animals, at 301-827-7571.

Sincerely,

for Steven D. Vaughn, DVM
Director
Office of New Animal Drug Evaluation
Center for Veterinary Medicine